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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/350,518	07/09/1999	JOHN C. REED	P-LJ-3578	8259
41552 7590 02/07/2007 MCDERMOTT, WILL & EMERY 4370 LA JOLLA VILLAGE DRIVE, SUITE 700 SAN DIEGO, CA 92122			EXAMINER SANG, HONG	
			ART UNIT 1643	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/07/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 09/350,518	Applicant(s) REED, JOHN C.	
	Examiner Hong Sang	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-14, 16, 20-27, 32-34, 36, 37, 44 and 50-66 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-14, 16, 20-27, 32-34, 36-37, 44 and 50-66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

RE: Reed

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/13/2006 has been entered.
2. Claims 11-14, 16, 20-27, 32-34, 36-37, 44 and 50-66 are pending and under examination.

Response to Arguments

3. The rejection of claims 11, 13-14, 16, 21-22, 24-27, 32, 34, 36-37, 44 and 50-61 under 35 U.S.C. 102(b) as being anticipated by Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) is maintained.

The response states that Turner et al. describes progressively higher percentages of overexpression of BAG-1 as breast tissue goes from benign (BBE, 47%) to noninvasive breast cancer (DCIS, 80%) to invasive breast cancer (IC, 93%), and in contrast, the claims recite that a high level of BAG-1 expression relative to a reference level of BAG-1 expression correlates positively with disease-free or overall survival, correlates negatively with tumor recurrence or spread, or classifies a patient as being less likely to suffer tumor metastasis or having an increased chance of survival (see

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response page 8, 2nd paragraph). The response states that Turner et al. concludes that "the subcellular location of BAG-1 overexpression may have prognostic importance with respect to survival of breast cancer patients" but provides no teaching that overexpression of BAG-1 would be prognostic for stage 1 or stage II breast cancer (see response page 8, last sentence). The response states that the survival difference of cytosolic staining for IC was not statistically significant at $p=0.06$ (see response page 9, 2nd paragraph). The Declaration of Dr. Reed attests that the survival difference of cytosolic staining for IC was not statistically significant and Turner et al. failed to show a significant correlation of BAG-1 expression in breast cancer cells with patient survival.

Applicants' arguments have been carefully considered but are not found persuasive. The Declaration of Dr. Reed and Exhibit 1 have been carefully considered but are insufficient to overcome the instant rejection. Turner et al. explicitly teach that the 10-year overall survival (OS) and distant disease free survival (DDFS) for breast cancer patients with overexpression of BAG-I in invasive carcinoma (IC) specimens was 75% and 70%, respectively, compared to 62% and 35% for tumors with low cytoplasmic BAG-I levels. Therefore, Turner et al. teach the method of correlating the disease-free or overall survival of an individual having a breast cancer tumor with the overexpression of BAG-1 protein. Because the instant specification teaches stage II of breast cancer involves either no lymph node involvement and a large primary tumor or initial lymph node involvement and a small primary tumor (see specification, page 25, lines 17-22), at least stage II breast cancer recited in the claims is invasive. Therefore, the invasive carcinoma in Turner's reference reads on the stage II breast cancer. The declaration of

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Dr. Reed states that Turner et al. describe the patient survival difference for nuclear staining of BAG-1 in benign breast epithelium (BBE) and no patient survival data were cited for nuclear BAG-1 expression in cancer cells. To response to this argument, whether Turner et al. teach the patient survival difference for nuclear staining of BAG-1 in cancer cells is immaterial because Turner et al. teach the patient survival difference for cytoplasmic staining BAG-1 in cancer cells, and nuclear BAG-1 is not a limitation of the claim. The Declaration of Dr. Reed further states that the patient survival difference of cytosolic staining of BAG-1 cited in Turner et al. for invasive cancer was not statistically significant ($p=0.06$). This is not found persuasive, because the standard for 102(b) reference is that the reference must teach every limitation of the claim. While the p value in Turner's method is 0.06, this is not a limitation of the claims. Moreover, the method described by Turner appears to be the same as one instantly claimed. One skilled in the art would expect to obtain the same results, such as p value as Turner et al. by performing the method described in the instant claims. Because Turner et al. teach all the limitation of the claims, the teachings of Turner et al. anticipate the instant inventions.

4. The rejection of claims 11-14, 16, 21-22, 24-27, 32-34, 36-37, 44 and 50-61 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Sano et al. (US patent NO. 5665539) is maintained.

The response states that Turner et al. does not teach or suggest the claimed methods for the same reasons set forth above, and Sano et al. does not cure the deficiencies of Turner et al., therefore, the claimed methods are unobvious over Turner et al. alone or in combination with Sano et al.

Applicants' arguments have been carefully considered but are not found persuasive. The reason that Turner's reference anticipates claims 11, 13-14, 16, 21-22, 24-27, 32, 34, 36-37, 44 and 50-61 has been set forth above (see paragraph 3). Therefore, the claimed methods are obvious in view of the teachings of Turner and Sano.

5. The rejection of claims 11, 13-14, 16, 20-22, 24-27, 32, 34, 36-37, 44 and 50-66 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Sauter et al. (British Journal of Cancer, 1997, 76(4): 494-501) is maintained.

The response states that Turner et al. does not teach or suggest the claimed methods for the same reasons set forth above, and Sauter et al. does not cure the deficiencies of Turner et al., therefore, the claimed methods are unobvious over Turner et al. alone or in combination with Sauter et al.

Applicants' arguments have been carefully considered but are not found persuasive. The reason that Turner's reference anticipates claims 11, 13-14, 16, 21-22, 24-27, 32, 34, 36-37, 44 and 50-61 has been set forth above (see paragraph 3).

Therefore, the claimed methods are obvious in view of the teachings of Turner and Sauter.

6. The rejection of claims 11, 13-14, 16, 21-27, 32, 34, 36-37, 44 and 50-61 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Takayama et al. (Cancer Res. 1998, 58: 3116-3131, IDS) is maintained.

The response states that Turner et al. does not teach or suggest the claimed methods for the same reasons set forth above, and Takayama et al. does not cure the deficiencies of Turner et al., therefore, the claimed methods are unobvious over Turner et al. alone or in combination with Takayama et al.

Applicants' arguments have been carefully considered but are not found persuasive. The reason that Turner's reference anticipates claims 11, 13-14, 16, 21-22, 24-27, 32, 34, 36-37, 44 and 50-61 has been set forth above (see paragraph 3). Therefore, the claimed methods are obvious in view of the teachings of Turner and Takayama.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 11, 13-14, 16, 20-22, 24-27, 32, 34, 36-37, 44 and 50-66 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Love (US Patent No. 6,221,622B1, Data of Patent 4/24/2001, earliest effective filing date 4/28/1998).

This rejection is directed to the claim limitation "detecting the level of BAG-1 protein expression in tumor cells from a body fluid".

The teachings of Turner et al. have been set forth before (see office action mailed on 10/20/05) as they apply to claims 11, 13-14, 16, 21-22, 24-27, 32, 34, 36-37, 44 and 50-61 (see paragraph 3 above)

Love teaches a method of obtaining fluids, marker substances and cellular material from single milk ducts in the breasts of a patient for cancer diagnosis (see column 3, lines 5-20), wherein the cellular material comprises epithelial cells from the lining of the duct, and the epithelial and other cells obtained by the method can be morphologically, histochemically, and/or immunohistochemically examined to determine if they are abnormal and to assess the likelihood of a cancer or pre-cancerous condition present in the cellular lining of the duct (see column 3, lines 35-45).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Turner et al. to detect BAG-1 in ductal fluid instead of in tissue sample for cancer prognosis in view of the teachings of Love. One would have been motivated to do so because unlike detecting BAG-1 in

tissue sample where the tumor must be first identified by other methods such as imaging, and biopsy must be performed, detecting BAG-1 in ductal fluid is non-invasive and it provides early cancer detection without the need of imaging the tumor before collecting the fluid. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to do so because Love teaches how to obtain cellular material from milk duct for breast cancer diagnosis and Turner teaches a method of prognosis of breast cancer by detecting BAG-1 protein in breast tumor cells.

Conclusion

9. No claims are allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

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Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
Jan. 30, 2007


CHRISTOPHER H. YAEN
PRIMARY EXAMINER